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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,383	01/08/2002	Hsien-Jue Chu	AM100249	3951

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 01/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/039,383	CHU ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 14-18* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-12 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 07/02/03 and 01/15/04 in response to the non-final Office Action mailed 01/07/03. With this, Applicants have amended the specification.

Petition Decision

2) The decision of 12/13/04 on Applicants' petition filed 11/01/04 has been noted. The decision on the petition states that the instant application is entitled to a filing date of 17 December 2001.

Status of Claims

3) Claim 13 has been canceled via the amendment filed 01/15/04.

Claims 10-12 and 15-17 have been amended via the amendment filed 01/15/04.

Claims 1-12 and 14-18 are pending.

Claims 10-12 and 14-17 are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

6) The objection to the specification made in paragraph 4 of the Office Action mailed 01/07/03 is withdrawn in light of Applicants' amendments to the specification.

Rejection(s) Moot

7) The rejection of claim 13 made in paragraph 5(g) of the Office Action mailed 01/07/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 13 made in paragraph 5(h) of the Office Action mailed 01/07/03

under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

9) The rejection of claim 13 made in paragraph 6 of the Office Action mailed 04/14/04 under 35 U.S.C § 112, first paragraph, as being non-enabling with regard to the scope, is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

10) The rejection of claim 10 made in paragraph 5(a) of the Office Action mailed 01/07/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claims 11 and 12 made in paragraph 5(b) of the Office Action mailed 01/07/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

12) The rejection of claims 11 and 12 made in paragraph 5(c) of the Office Action mailed 01/07/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

13) The rejection of claim 16 made in paragraph 5(d) of the Office Action mailed 01/07/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claim 17 made in paragraph 5(e) of the Office Action mailed 01/07/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

15) The rejection of claim 17 made in paragraph 5(f) of the Office Action mailed 01/07/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

16) The rejection of claims 11, 12 and 14-17 made in paragraph 5(h) of the Office Action mailed 04/14/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

17) The rejection of claims 10-12 and 14-17 made in paragraph 6 of the Office Action mailed 04/14/04 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is

withdrawn. A new ground of rejection(s) is set forth herebelow.

Rejection(s) under 35 U.S.C § 103

18) Claims 10-12 and 14-16 are rejected under 35 U.S.C § 103(a) as being unpatentable over Petersen *et al.* (WO 92/03157) and Byars *et al.* (*Vaccine* 5: 223-228, 1987) in view of Liem *et al.* (US 20020114817, filed 09/29/1999).

The reference of Liem *et al.* is used in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C. § 102 and accordingly is not disqualified under U.S.C. 103(a).

Petersen *et al.* disclosed a method of immunizing and protecting a swine against infection by *Mycoplasma hyopneumoniae* comprising administering to the swine at least one (i.e., single) dose of a bacterin, i.e., a virulent *M. hyopneumoniae* that is inactivated with binary ethyleneimine, which bacterin prevents mycoplasmal pneumonia (see pages 4-6; page 8; page 12; Example 2; first paragraph on page 29; Table 3; claims 20-22; and page 32). The bacterin comprises physiologically acceptable carrier or mineral oil and an adjuvant such as 0.2% w/v Carbopol, a polymer of acrylic acid (see last paragraph on page 7; last full paragraph on page 19; page 30; and page 8). It is taught that effective amounts of the adjuvant may be readily determined so as to optimize the potentiation effect of the adjuvant on the immune response of an animal vaccinated with the bacterin (see page 8). The immunizing amount of the vaccine includes at least about 10^9 *M. hyopneumoniae* DNA cell equivalents per mL of the bacterin (see last paragraph on page 8). The vaccine is administered intramuscularly or through various routes (see page 12). The vaccine comprises one or more of other antigenic substances capable of inducing a protective immune response against *M. hyopneumoniae* or against other disease-causing agents (see third full paragraph on page 13).

Petersen *et al.* differ from the instant invention in not having a metabolizable oil and a polyoxyehtylene-polypropylene block copolymer admixed with the Carbopol adjuvant.

However, the use of an adjuvant mixture in a veterinary vaccine wherein the adjuvant mixture contains a metabolizable oil comprising trepene hybrocarbon, such as, squalene or squalane, and a polyoxyehtylene-polypropylene block copolymer, such as, PLURONIC L121 was well known in the art at the time of the invention. For instance, Byars *et al.* taught adding a

safe, efficacious, non-allergenic, metabolizable and easily prepared adjuvant, SAF-1, which comprises10% squalene or squalane, plus 2.5% v/v PLURONIC L121 to vaccines for eliciting both humoral and cell-mediated immunity. Byars *et al.* taught that this new adjuvant formulation avoids the difficulties encountered with Freund's adjuvant, such as, non-approval for continued human use and formation of sterile abscesses; and also the carcinogenic nature of Arlacel A (see pages 223 and 224). Byars *et al.* expressly recommended the use of their adjuvant formulation with a wide variety of antigens in human and veterinary vaccines (see page 223 and 227). Byars *et al.* taught that the adjuvant formulation is not only used with soluble antigens but also with inactivated vaccines (see page 226).

Liem *et al.* showed the routine and conventional practice of using a combination or mixture of art known adjuvants, such as, squalene or squalane and Pluronic along with known bacterial vaccines. Liem *et al.* taught the preferable embodiment of using a combination adjuvant comprising oils, polymers, and block co-polymers. See section [0030].

Given the routine and conventional mixing of several art-known adjuvants including oils, polymers and block co-polymers in an art-known vaccine as taught by Liem *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Byar's SAF1 adjuvant formulation comprising squalene or squalane and PLURONIC L121 mixture to the Carbopol-containing *M. hyopneumoniae* bacterin vaccine used in Petersen's method to produce the instant invention with a reasonable expectation of success, because Byars *et al.* expressly taught that their safe, efficacious, non-allergenic, metabolizable, and easily prepared SAF-1 adjuvant formulation is useful in both veterinary and human vaccines with a wide variety of antigens. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of further enhancing the immunogenicity of Petersen's vaccine in Petersen's method of protection by promoting the elicitation of both humoral and cell-mediated immunity to *M. hyopneumoniae* bacterin while avoiding safety related difficulties such as formation of sterile abscesses and carcinogenicity associated with other art known adjuvants as taught by Byars *et al.*

Claims 10-12 and 14-16 are *prima facie* obvious over the prior art of record.

19) Claim 17 is rejected under 35 U.S.C § 103(a) as being unpatentable over Petersen *et al.*

(WO 92/03157) as modified by Byars *et al.* (*Vaccine* 5: 223-228, 1987) and Liem *et al.* (US 20020114817, filed 09/29/1999) as applied to claim 10 above, and further in view of Burkhardt *et al.* (US 6,342,231, filed 07/01/1998) and Potter *et al.* (US 5,534,256).

The teachings of Petersen *et al.* as modified by Byars *et al.* and Liem *et al.* are disclosed above, which do not teach co-administering the *M. hyopneumoniae* bacterin preparation with an additional bacterin such as *Haemophilus parasuis* bacterin as recited in claim 17.

However, Burkhardt *et al.* taught that inactivated bacterin vaccines of *Haemophilus parasuis* were commercially available. Burkhardt *et al.* further taught that *Haemophilus parasuis* is a porcine pathogen that causes a contagious disease of high morbidity in pigs (see fourth full paragraph in column 1 and lines 39 and 40 in column 1.

Potter *et al.* disclosed that other bacterial antigens can be 'combined' with pharmaceutical compositions comprising one bacterial antigen, to afford broad spectrum immunity against a variety of diseases (see column 1, first and last paragraphs).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine Burkhardt 's commercially available porcine *Haemophilus parasuis* bacterin to Petersen's *M. hyopneumoniae* bacterin for use in Petersen's method as modified by *Byars et al.* and *Liem et al.* to produce the instant invention, with a reasonable expectation of success. Given that both *M. hyopneumoniae* bacterin and *Haemophilus parasuis* are meant for immunizing porcine animals, one of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a method for protecting porcine hosts with a more effective multivalent bacterin composition that advantageously induces a broad spectrum immunity against more than one swine disease as taught by Potter *et al.*

Claim 17 is *prima facie* obvious over the prior art of record.

Remarks

20) Claims 10-12 and 14-17 stand rejected.

21) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives

transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses or papers is (571) 273-8300.

22) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

23) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

January, 2005

SD

S. DEVI, PH.D.
PRIMARY EXAMINER